REMARKS

Applicants have amended claims 1, 45 and 47 and canceled claim 2 as described in detail below.

Applicants respectfully disagree with the statements at page 2 of the Office Action that the elections were made without traverse. Applicants' response clearly stated that the elections were made with traverse and that there was no undue burden on the Examiner to search the subject matter of Groups I and II.

The class and subclasses listed for search are identical. According to M.P.E.P. Sec. 803 "[I]f the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions". Separate classification, separate status in the art or different field of search has not been shown and therefore the prima facie showing as a basis for restriction/election has not been met. Therefore, the supposed errors (no undue burden to search) were distinctly and specifically pointed out and each restriction/election response should be treated as having been made with traverse.

At pages 3-4 of the Office Action, claims 45 and 47 have been rejected under 35 U.S.C. § 112, first paragraph because of lack of enablement. For brevity, reference is made to pages 3-4 of the Office Action for the complete reasons for rejection.

While Applicants respectfully disagree with and traverse this rejection, claims 45 and 47 have been amended to remove the phrase "or prevention" to expedite allowance of the present application, without prejudice to filing of one or more divisional patent applications directed to the canceled subject matter thereof.

Accordingly, Applicants respectfully request that the rejection of claims 45 and 47 under 35 U.S.C. § 112, first paragraph be reconsidered and withdrawn.

At pages 4-5 of the Office Action, claims 1, 11, 18-20, 35-37, 42-45 and 47 have been rejected under 35 U.S.C. § 112, first paragraph because of lack of enablement of other sterol absorption inhibitors. For brevity, reference is made to pages 4-5 of the Office Action for the complete reasons for rejection.

While Applicants respectfully disagree with and traverse this rejection, claim 1 has been amended to clarify that, in one embodiment, the sterol absorption inhibitor is that of formula (I), in order to expedite allowance of the present application, without prejudice to filing of one or more divisional patent applications directed to the

canceled subject matter thereof. Claims 11, 18-20, 35-37, 42-45 and 47 depend from claim 1.

Accordingly, Applicants respectfully request that the rejection of claims 1, 11, 18-20, 35-37, 42-45 and 47 under 35 U.S.C. § 112, first paragraph be reconsidered and withdrawn.

At pages 6-8 of the Office Action, claims 1-3, 11, 18-20, 35-37, 42-45 and 47 have been rejected under 35 U.S.C. §103(a) as obvious over EP 0720599 ("Rosenblum et al.") and WO 99/47123 ("Ullah") in view of Frei (Proc Soc Exp Biol Med. 1999 Dec; 222(3): 196-204).

For brevity, the reasons for rejection are not repeated herein but reference is made to the outstanding Office Action.

Applicants respectfully traverse this rejection and request that the rejection be reconsidered and withdrawn.

When making a rejection under 35 U.S.C. § 103, the Examiner has the burden of establishing a prima facie case of obviousness. In re Fritch, 23 U.S.P.Q.2d 1780, 1783 (Fed. Cir. 1992). The Examiner can satisfy this burden only by showing an objective teaching in the prior art, or knowledge generally available to one of ordinary skill in the art, which would lead an individual to combine the relevant teachings of the references [and/or the knowledge] in the manner suggested by the Examiner. Id.; In re Fine, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988).

The mere fact that the prior art could be modified does not make the modification obvious unless the prior art suggests the desirability of the modification. In re Fritch, 23 U.S.P.Q.2d at 1784; In re Laskowski, 10 U.S.P.Q.2d 1397, 1398 (Fed. Cir. 1989); In re Gordon, 221 U.S.P.Q. 1125, 1127 (Fed. Cir. 1984).

"It is impermissible to use the claimed invention as an instruction manual or 'template' to piece together the teachings of the prior art so that the claimed invention is rendered obvious....'[o]ne cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.'" In re Fritch, 23 U.S.P.Q.2d at 1784 (quoting In re Fine, 5 U.S.P.Q.2d at 1600).

"The ultimate determination of patentability must be based on consideration of the entire record, by a preponderance of evidence, with due consideration to the persuasiveness of any arguments and any secondary evidence." Manual of Patent

Examining Procedure, (Rev. 1, Feb. 2003) § 716.01(d) and In re Oetiker, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992).

It is respectfully submitted that the combination of the references cited as rendering the claimed invention obvious is improper because there is no suggestion in the cited references to combine the claimed components of sterol absorption inhibitor (such as that of Formula (I) (e.g., ezetimibe)) and blood modifier such as aspirin.

Applicants wish to emphasize that claim 1 does not require the presence of a third component, such as a statin, although such third component optionally can be present.

With respect to patentability of a composition or combination of a sterol absorption inhibitor and blood modifier such as aspirin (*without the presence of a statin*), Rosenblum does not suggest or disclose combinations of a sterol absorption inhibitor and blood modifier such as aspirin. Ullah does not suggest or disclose combinations of a sterol absorption inhibitor and blood modifier such as aspirin. Neither Rosenblum, Ullah nor Frei provides motivation for substituting a sterol absorption inhibitor for the statin disclosed in Ullah. Ezetimibe sterol absorption inhibitor has a mechanism of action that differs from those of other classes of cholesterol-reducing compounds (HMG CoA reductase inhibitors (statins)). Id.

Ezetimibe reduces blood cholesterol by inhibiting the absorption of cholesterol by the small intestine. See ZETIA™ (ezetimibe) Tablets Package Insert at column 1 (Merck/Schering-Plough Pharmaceuticals) (October 2002) included in the Information Disclosure Statement filed concurrently herewith (copy attached for the Examiner's convenience as Exhibit A).

The cholesterol content of the liver is derived predominantly from three sources. Id. The liver can synthesize cholesterol, take up cholesterol from the blood from circulating lipoproteins, or take up cholesterol absorbed by the small intestine. Id. Intestinal cholesterol is derived primarily from cholesterol secreted in the bile and from dietary cholesterol. Id.

Ezetimibe does not inhibit cholesterol synthesis in the liver (like HMG CoA reductase inhibitors). Id. Instead, ezetimibe localizes and appears to act at the brush border of the small intestine and inhibits the absorption of cholesterol, leading to a decrease in the delivery of intestinal cholesterol to the liver. Id. This causes a

reduction of hepatic cholesterol stores and an increase in clearance of cholesterol from the blood. Id.

Ezetimibe does not operate by the same mechanism as either cholesterol biosynthesis inhibitors. Because of the difference of the way that each component of the presently claimed combination acts, it is respectfully submitted that the rejection is based upon an improper combination of references. There is no suggestion or motivation in the references to substitute the claimed sterol absorption inhibitor for the statin of Ullah that operates by a different mechanism.

With regard to the claimed triple combination of sterol absorption inhibitor, aspirin and statin, the cited references provide no motivation for adding a separate sterol absorption inhibitor that acts by a different mechanism to the combination of statin and aspirin disclosed by Ullah.

With regard to a quadruple combination of sterol absorption inhibitor, aspirin, statin and antioxidant, the cited references provide no motivation for adding a separate sterol absorption inhibitor that acts by a different mechanism to the combination of statin and aspirin disclosed by Ullah or to further include an antioxidant.

There is no suggestion or motivation in the references to combine the claimed components that operate by these different mechanisms.

Accordingly, reconsideration and withdrawal of the §103(a) rejection is respectfully requested.

In view of the foregoing remarks, it is respectfully submitted that all of the pending claims in the present application comply with the requirements of § 112 and patentably distinguish over the cited prior art. Accordingly, examination on the merits for the pending claims, reconsideration and withdrawal of the rejections and an early Notice of Allowance are respectfully requested.

Respectfully submitted,

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